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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,735	12/28/2001	Katsutoshi Sasaki	5.1196	7344

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EXAMINER	
PROUTY, REBECCA E	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 07/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/019,735	SASAKI ET AL.	
	Examiner	Art Unit	
	Rebecca E. Prouty	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-39* is/are pending in the application.

4a) Of the above claim(s) *34-37 and 39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-33 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The previous Office Action restricted the claims but improperly based the restriction on US restriction practice. As the instant case was filed under 35 USC 371, the restriction requirement should have been made using lack of unity practice as defined by PCT Rule 13.1. As the groupings of claims would not change, they are not repeated herein, however, the following are reasons for restriction under the lack of unity standard: The inventions listed as Groups I-LVIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The only shared technical feature of these groups is that they all relate to nucleic acids encoding a -acetylglucosaminyltransferase. However this shared technical feature is not a special technical feature as defined by PCT Rule 13.2 as it does not define a contribution over the art. Sasaki et al. (PNAS 94:14294, 1997) and Zhoud et al. (PNAS 96:406, 1999) each teach nucleic acids encoding a β1,3-N-acetylglucosaminyltransferase. Furthermore, the protein of SEQ ID NO:2 is not a special technical feature linking the groups as the protein of SEQ ID NO:2 is not a feature which defines a contribution over the prior art as a

protein identical to SEQ ID NO:2 is encoded taught by Kato et al. (WO 98/21328).

Applicant's election with traverse of Group XIII, Claims 31-33 and 38 in the response filed 5/28/04 is acknowledged. Claims 1-30 and 40-61 have been canceled. Claims 31-39 are at issue and are present for examination.

Applicants argue that the examiner has made no showing that the amino acid sequences among Groups I-IV are separately patentable, or that the nucleotide sequences among Groups V-VIII are separately patentable. However, as discussed above these proteins and nucleic acids are clearly separately patentable as each of them is structurally distinct and the only shared feature among them is that they are all β1,3-N-acetyl-glucosaminyltransferases or nucleic acids encoding a β1,3-N-acetylglucosaminyltransferase. However this shared feature is not a special technical feature as defined by PCT Rule 13.2 as it does not define a contribution over the art.

Applicants further traverse the restriction on the basis that the MPEP 803.04 recites that in most cases up to ten independent and distinct nucleotide sequences will be examined in a single application without restriction and applicants submit that because no more than 4 independent and distinct

sequences are claimed, all the sequences should be examined together. Applicants traversal is not found persuasive for the following reasons: Applicant is reminded that the MPEP recites **up to 10** distinct nucleotide sequences not **at least 10** nucleotide sequences, and while applicants assert that they are claiming no more than 4 independent and distinct sequences, they are in fact claiming many more than 4 independent and distinct sequences when one considers they are claiming each of SEQ ID NOs: 5-8 as well as those which encode SEQ ID NOS:1-4 as well as those which encode proteins which have one or more amino acids added, deleted or substituted in the sequences of SEQ ID NOS:1-4. Thus applicants are claiming many more than 4 independent and distinct sequences. Thus these inventions are distinct for the reasons given previously.

Claims 34-37 and 39 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 5/28/04. However, in view of the use of the incorrect standard as basis for the restriction in the previous action, the restriction requirement

is not made final herein in order to give applicants a chance to traverse the reasons given for lack of unity herein.

Claims 31-33 and 38 are objected to as reciting non-elected subject matter.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "Process for producing carbohydrates using β1,3-N-acetyl-glucosaminyltransferase".

Claim 32 is objected to because of the following informalities: the words "are allowed" at the end of (c) should be deleted and the word "the" should be inserted prior to "N-acetylglucosamine residue" in line 10. Appropriate correction is required.

Claim 33 is objected to because of the following informalities: the word "and" should be inserted following the final recovering step. Appropriate correction is required.

Claims 31-33 and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 31 and 33 (upon which Claims 32 and 38 depend) lack antecedent basis for the recitation of "the sugar chain synthesizing agent" in line 3 of Claim 31 and line 4 of Claim 33. It is suggested that the claims be amended to recite "a sugar chain synthesizing agent"

These claims are directed to methods of using a genus of β1,3-N-acetylglucosaminyltransferases and GlcNac β1,4-galactosyltransferases. The specification teaches the structure of only a few representative species of β1,3-N-acetyl-glucosaminyltransferases and GlcNac β1,4-galactosyltransferases. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the enzymatic function. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 31-33 and 38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of using a β1,3-N-acetylglucosaminyltransferase comprising residues 45-372 of SEQ ID NO:2 and GlcNac β1,4-

galactosyltransferases disclosed by Almeida et al. or Schwientek et al., does not reasonably provide enablement for methods of using any β1,3-N-acetylglucosaminyltransferase or any GlcNac β1,4-galactosyltransferase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claim are so broad as to encompass methods of using any β1,3-N-acetylglucosaminyltransferase or any GlcNac β1,4-galactosyltransferase. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of β1,3-N-acetyl-glucosaminyltransferases or GlcNac β1,4-galactosyltransferases broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in

this case the disclosure is limited to the amino acid sequence of four β1,3-N-acetylglucosaminyltransferases and the nucleotide sequences encoding them and the citation of two references disclosing four known GlcNac β1,4-galactosyltransferases amino acid sequences.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass use of any β1,3-N-acetyl-glucosaminyltransferase or any GlcNac β1,4-galactosyltransferase because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting β1,3-N-acetylglucosaminyltransferase or GlcNac β1,4-

galactosyltransferase activity; (B) the general tolerance of β1,3-N-acetylglucosaminyltransferases and GlcNac β1,4-galactosyltransferases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any β1,3-N-acetylglucosaminyltransferase or GlcNac β1,4-galactosyltransferase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including use of any β1,3-N-acetyl-glucosaminyltransferase or any GlcNac β1,4-galactosyltransferase. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of β1,3-N-acetyl-glucosaminyltransferases and GlcNac β1,4-galactosyltransferases having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly,

extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 31 and 38 rejected under 35 U.S.C. 102(b) as being anticipated by either of Sasaki et al. or Zhou et al.

Sasaki et al. teach the cloning and expression of a human β1,3-N-acetyl-glucosaminyltransferase gene and the use of the recombinant protein for the enzymatic addition of a GlcNac residue to the galactose residue at the non reducing end of lactose, N-acetyllactosamine residues attached to α_1-acid glycoprotein and lacto-N-neo-tetraose. Although the β1,3-N-acetylglucosaminyltransferase of Sasaki et al. is not identical to SEQ ID NO:2, it clearly meets the limitation of comprising an

amino acid sequence in which one or more amino acids of SEQ ID NO:2 are deleted, substituted or added.

Zhou et al. teach the cloning and expression of a human β1,3-N-acetyl-glucosaminyltransferase gene and the use of the recombinant protein for the enzymatic addition of a GlcNac residue to the galactose residue at the non reducing end of a variety of substrates (see Table 1) including lactose, N-acetyllactosamine and lacto-N-neo-tetraose. Although the β1,3-N-acetylglucosaminyltransferase of Zhou et al. is not identical to SEQ ID NO:2, it clearly meets the limitation of comprising an amino acid sequence in which one or more amino acids of SEQ ID NO:2 are deleted, substituted or added.

Claims 31-33 and 38 rejected under 35 U.S.C. 102(b) as being anticipated by Di Virgillio et al.

Di Virgillio et al. teach the enzymatic production of poly-N-acetyllactosamines by the use of sequential use of a β1,3-N-acetylglucosaminyltransferase and a GlcNac β1,4-galactosyltransferase. Although the structure of the β1,3-N-acetylglucosaminyltransferase of Di Virgillio et al. is not given and is likely not identical to SEQ ID NO:2, it clearly meets the limitation of comprising an amino acid sequence in

which one or more amino acids of SEQ ID NO:2 are deleted, substituted or added.

Claims 31 and 38 rejected under 35 U.S.C. 102(e) as being anticipated by Fukuda et al. (WO 01/85177).

Fukuda teach the cloning and expression of a β1,3-N-acetylglucosaminyltransferase identical to SEQ ID NO:2 and its use for the enzymatic addition of a GlcNac residue to the galactose residue at the non reducing end of a acceptor molecule having the structure (Galβ1→3GalNAc→R) where the acceptor can contain other sugar residues or be part of a glycoprotein such as CD34 (see page 38). The disclosure of the β1,3-N-acetylglucosaminyltransferase of Fukuda and its use was first disclosed in US application 09/569,320, filed 5/11/00. While it is noted that the effective date of Fukuda et al. falls after applicants claimed foreign priority date, applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at

> the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 32 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Di Virgillio et al. in view of Fukuda et al. (WO 01/85177)

Fukuda et al. and Di Virgillio et al. are discussed above. The synthesis of Di Virgillio et al. does not utilize the β1,3-N-acetylglucosaminyltransferase of SEQ ID NO:2 and Fukuda et al. do not disclose the use of the β1,3-N-acetylglucosaminyltransferase identical to SEQ ID NO:2 of the instant invention for the synthesis of poly-N-acetyllactosamines. However, Di Virgillio et al. explicitly suggest using recombinant glycosyltransferases in the synthetic reaction systems disclosed and in other such systems (see page 360). Therefore, as Fukuda et al. teach the recombiant production of an enzyme which catalyzes the identical reaction

to the β1,3-N-acetylglucosaminyltransferase used by Di Virgillio et al. it would have been obvious to one of skill in the art to use the enzyme of Fukuda et al. in the poly N-acetyllactosamine synthesis of Di Virgillio et al. as recombinant production would provide large quantities of the enzyme.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (571) 272-0937. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Rebecca Prouty
Primary Examiner
Art Unit 1652